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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/933,638	08/20/2001	Aleksey G. Kazantsev	01997-289001	6696

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EXAMINER	
DESAI, ANAND U	
ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 11/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/933,638	KAZANTSEV ET AL.	
	Examiner	Art Unit	
	Anand U. Desai, Ph.D.	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-27,31-33,36-38,40-43 and 46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-27,31-33,36-38,40-43 and 46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. 20061020
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This office action is in response to Amendment filed on September 1, 2006. Claims 1-20, 28-30, 34, 35, 39, 44, and 45 have been cancelled. Claims 21-27, 31-33, 36-38, 40-43, and 46 are currently pending and are under examination.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

3. Claim 22 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. It is unclear if the phrase, "the polypeptide" in claim 22 is referring to the first, second, or the third domain. Amended claim 21 now recites the first domain and/or the second domain comprises a polypeptide, as does the third domain. Which polypeptide is claim 22 referring to?

5. Claims 21-27, 31-33, 36-38, 40-43, and 46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, at the time the invention was made, of the specific subject matter claimed. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966." *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

MPEP § 2163 further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163 does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative

species that encompass the genus. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The factors considered in the Written Description requirement are (1) *level of skill and knowledge in the art*, (2) *partial structure*, (3) *physical and/or chemical properties*, (4) *functional characteristics alone or coupled with a known or disclosed correlation between structure and function*, and the (5) *method of making the claimed invention*. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163.

In the instant case, the claims are drawn to a therapeutic agent comprising a first domain that binds a first protein, the first protein having at least seven consecutive glutamine residues, a second domain that binds a second protein, the second protein having at least seven consecutive glutamine residues; and a third domain, wherein the third domain consists of a polypeptide comprising an alpha-helical region or a beta-sheet, and separates the first domain from the second domain. The first domain and the second domain comprise a polypeptide comprising at least 80% glutamine residues. Some claims are drawn to a therapeutic agent wherein the first **or** the second domains can comprise the first 17 amino acid residues of the Huntingtin protein fused

to 25 consecutive glutamine residues, and optionally, a sufficient number of hydrophilic amino acid residues to increase the solubility of the therapeutic agent, the hydrophilic amino acid residues including at least one aspartic acid or glutamic acid residue. Claims are also drawn to a therapeutic agent comprising a first domain that binds a first protein, the first protein having at least seven consecutive glutamine residues, a second domain that binds a second protein, the second protein having at least seven consecutive glutamine residues; and a third domain, wherein the third domain consists of a polypeptide comprising an alpha-helical region or a beta-sheet, and separates the first domain from the second domain, wherein the first and second domain are identical. Some claims are drawn to a therapeutic agent, wherein the third domain consists of a polypeptide comprising a fragment of the sequence of a TATA-binding protein, such that the TATA-binding protein consists of the sequence of SEQ ID NO: 12.

(1) Level of skill and knowledge in the art:

The level of skill in this art is high and is at least that of a doctoral scientist with several years of experience in the art of producing therapeutic fusion polypeptides. Marsh et al. (cited previously) does describe the unpredictability in determining the functional effects of fusion proteins; A 26 amino acid myc/flag epitope added to a cytotoxic polyglutamine polypeptide (Q108) reduced lethality, "from 100% lethality to near zero lethality with the elav or dppblk drivers...the toxic effect of Q108 can be profoundly altered by the inclusion of additional amino acids." (see page 21, right hand column, PolyQ cytotoxicity is modified by protein context section).

(2) Partial structure: / (3) Physical and/or chemical properties:

The examples describe the suppression of protein aggregation using fusion polypeptides constructed with a third domain comprising alpha helical sequences from TATA-binding protein, identified as H1/H2 (SEQ ID NO: 6), H2/H3 (SEQ ID NO: 7), and H3/H4 (SEQ ID NO: 8).

(4) Functional characteristics: / (5) Method of making the claimed invention:

The specification describe the suppression of protein aggregation using fusion polypeptides, but provides no guidance as to selecting any fragments of the sequence of a TATA-binding protein, neither does the specification describe any therapeutic agents where the first and second domains are other than the first 17 amino acids residues of Huntingtin protein fused to 25 consecutive glutamine residues. The breadth of the claim encompass an alternative first or second domain that is described by a functional characteristic of binding a protein having at least seven consecutive glutamine residues.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad genus. Claims are broadly generic to all possible polypeptides that can functionally bind proteins having at least seven consecutive glutamine residues encompassed by the claims. The possible variations are enormous. Since the MPEP states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the respective first, second, and third domains beyond those disclosed in the examples in the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus since the specification does not provide any examples of other

polypeptides comprising at least 80% glutamine residues that can bind a protein having at least seven consecutive glutamine residues.

While having written description of H1/H2, H2/H3, and H3/H4 helical segments of the TATA-binding protein linked with the first 17 amino acid residues of Huntingtin protein fused to 25 consecutive glutamine residues identified in the specification examples, the specification is devoid of any description of all amino acid sequences of TATA-binding protein encompassed by fragments thereof that qualify for the functional characteristics. The specification is also devoid of any other polypeptides for the first and second domains that can be separated by the helical segments of the TATA-binding protein, when the first and second domains are not the first 17 amino acid residues of Huntingtin protein fused to 25 consecutive glutamine residues. The breadth of the claim is not described, because the structure for the first and second domain is unknown when the polypeptide is not the first 17 amino acid residues of Huntingtin protein fused to 25 consecutive glutamine residues.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Conclusion

6. No claims are allowed.

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anand U. Desai, Ph.D. whose telephone number is (571) 272-0947. The examiner can normally be reached on Monday - Friday 9:00 a.m. - 5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on (517) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

November 8, 2006

ROBERT A. WAX
PRIMARY EXAMINER